

Amendments to the Specification

Please replace the paragraph beginning at page 1, line 3 with the following amended paragraph:

Funding for work described herein was provided in part by the National Institutes of Health, grant no. HL15728. ~~The~~ the federal government, ~~which~~ has certain rights in the invention.

Please replace the paragraph beginning at page 4, line 3 with the following amended paragraph:

The modified GLA domain of factor VII, factor VIIa, and active site modified factor VIIa may contain a substitution at amino acids 11, 29, 33, 34, or 35, and combinations thereof. For example, a glutamine, glutamic acid, aspartic acid, or an ~~asparagine~~ asparagine residue can be substituted at amino acid 11, a glutamic acid or phenylalanine residue can be substituted at amino acid 29, or a glutamic acid residue can be substituted at amino acid 33, and combinations thereof such as substitutions at 11 and 29, 11, 29, and 33, and 11 and 33. Substitution of a glutamine residue at amino acid 11 is particularly useful. In one embodiment, a glutamine residue is substituted at amino acid 11 and a glutamic acid residue is substituted at amino acid 33. The modified GLA domain further can include at least one hydrophobic residue at amino acids 34 or 35. Phenylalanine, leucine, or isoleucine residue may be substituted at amino acid 34, and/or an aspartic acid or glutamic acid residue at amino acid 35.

Please replace the paragraph beginning at page 5, line 5 with the following amended paragraph:

In another aspect, the invention features a vitamin K-dependent polypeptide that includes a modified GLA domain that enhances membrane binding affinity and activity of the polypeptide. The modified GLA domain of such a polypeptide includes at least one amino acid insertion at amino acid 4. The polypeptide can be factor VII or VIIa, protein C or activated

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protein C, factor X or Xa, or protein S. For example, the polypeptide can be factor VII or Ha VIIa, or protein C or activated protein C, and can include the insertion of a tyrosine or glycine residue.

Please replace the paragraph beginning at page 13, line 14 with the following amended paragraph:

Factor VII or VIIa modified in these manners has a much higher affinity for membranes than the native or wild type polypeptide. Factor VII or Ha VIIa also have a much higher activity in autoactivation, in factor Xa generation and in several blood clotting assays. Activity is particularly enhanced at marginal coagulation conditions, such as low levels of tissue factor and/or phospholipid. For example, modified factor VII is about 4 times as effective as native VIIa at optimum thromboplastin levels, but is about 20-fold as effective at 1% of optimum thromboplastin levels. Marginal pro-coagulation signals are probably most predominant *in vivo*. Presently available clotting assays that use optimum levels of thromboplastin cannot detect clotting time differences between normal plasma and those from hemophilia patients. Clotting differences between such samples are only detected when non-optimal levels of thromboplastin or dilute thromboplastin are used in clotting assays.

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